Radical Based Strategies for the C-C and C-Heteroatom Bond Formations

By

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Origin of the research problem:

From early ages, the ability of natural systems to connect solar energy for the creation of matter has been attracting mankind to mimic and reproduce the system in context of chemical synthesis. The journey of using photochemical reactions for the synthesis of organics have started since time immemorial and until 1980s most of the photochemical reactions exploited stoichiometric amount of photoactive molecular entity.[1]

Visible light driven photoredox processes have been an attractive choice for synthesizing heterocycles as in to develop sustainable synthetic processes.[2] So a continuous effort have been made to modify this mode of synthetic transformations, and only recently, a number of transition metal complexes are being evolved as redox-active and show absorption in the visible region of solar spectrum that effectively catalyzes the light driven organic transformations. Use of metals mainly ruthenium and iridium comprising pyridyl-based complexes like $[Ru(bpy)_3]^{2+}$, $[Ir(ppy)_3]$, $[Ir(ppy)_2(dtbbpy)]^+$ etc. are commonly employed as efficient visible light photocatalysts for organic transformations that are mostly mediated by single-electron transfer processes.[3] Despite the excellent photophysical properties of ruthenium and iridium polypyridyl complexes in visible light photocatalysis, the compounds are expensive and potentially toxic, causing disadvantages on a larger scale.[4] Organic dyes have been used as an attractive substitute to transition metal complexes in Photoredox catalysis.[5] They are less expensive and less toxic, easy to handle and even better performs in compare to organometallic and inorganic catalysts in some cases.[6] Particularly, eosin Y has been widely used as an organo-photocatalyst in synthetic transformations.[7]

In performing a visible light driven photocatalytic transformation, the typical irradiation sources of light used are LEDs or household lamps, which are cheaper and easier to handle without any special care to be taken off in compare to specialized UV reactors used in classical photochemistry. The general working principle of a photo catalyst is depicted in Fig.1.

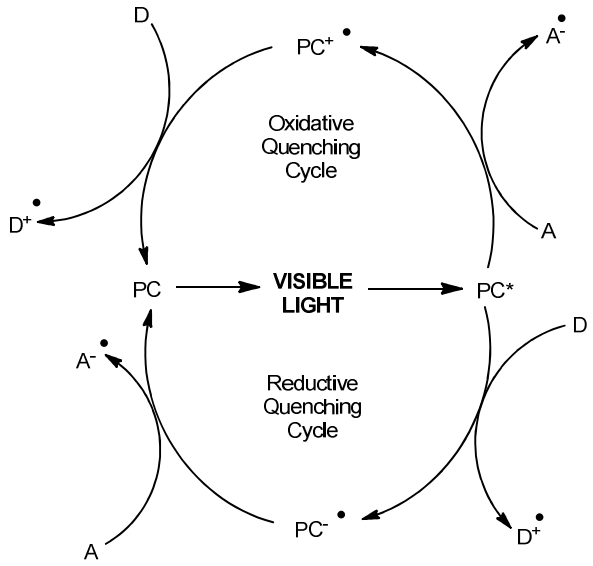


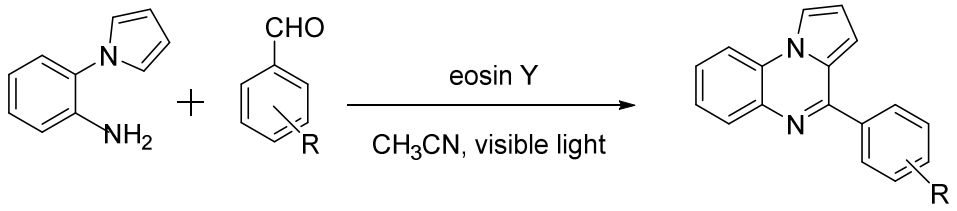
Fig.1: General working principle of photocatalyst

Objective(s) of the work:

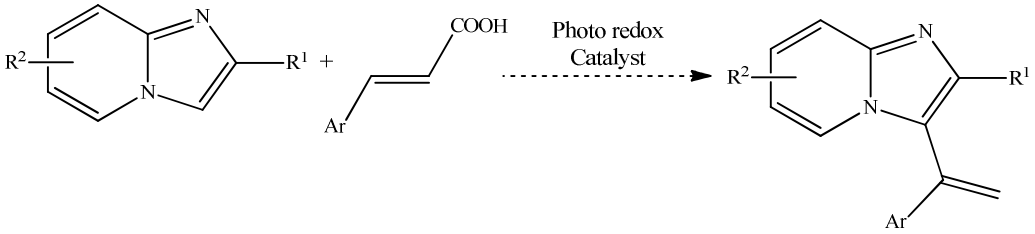
Keeping green chemistry aspect in organic synthesis my objective is to develop simple and efficient protocols for the C-C and C-heteroatom bond formations using photoredox catalysts via radical mechanism.Various biological active heterocyclic compounds have been synthesized using this methodology.

Methodology:

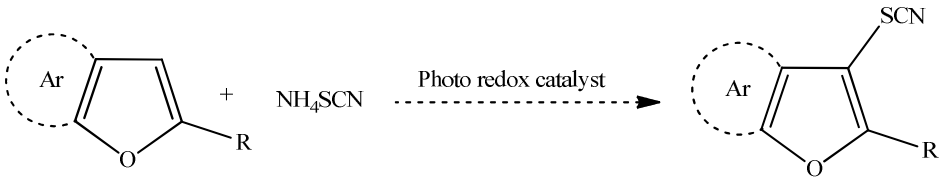
Quinoxaline derivatives are an important class of biologically active nitrogen heterocycles which exhibit a wide range of pharmacological profiles.[8]3 In particular, pyrrolo[1,2-a]quinoxalines substituted at the C-4 position have shown diverse biological activities such as anti-cancer,[9]4 anti-malarial,[10]5 and antiproliferative[11]6 activities. Due to the wide range of applications, a signicant number of synthetic protocols[12]12 have been devised in the past for the preparation of various pyrrolo[1,2-a]- quinoxaline derivatives.[13]16 But these methods still suffer from a number of demerits such as long reaction times, harsh reaction conditions and use of hazardous organic solvents. Therefore,herein we have been developed an efficient, economical, environmentally friendly method for the synthesis of quinoxaline derivatives using visible light and eosin Y as a photocatalyst.



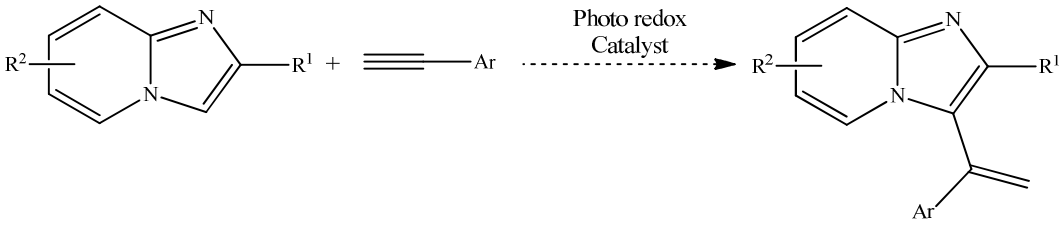
Future prospect:



Scheme 1: α-vinylation of imidazopyridine.



Scheme 2: thiocyanation of furan derivatives.



Scheme 3: C-2 alkylation of imidazopyridine using alkyne derivatives.

Notes and references:

1. A. G. Griesbeck, M. Oelgemöller, F. Ghetti, Eds. CRC *Handbook of Organic Photochemistry and Photobiology*, 3rd ed.; CRC Press: Boca Raton, **2012**.

2. (a) D. P. Hari, B. König, *Angew. Chem., Int. Ed.*, **2013**, *52*, 4734. (b) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.,* **2012**, *41*, 7687. (c) T. Hering, D. P. Hari, B. König, *J. Org. Chem.,* **2012**, *77*, 10347. (d) M. Rueping, C. Vila, T. Bootwicha, *ACS Catal.,* **2013**, *3*, 1676.

3. (a) J. D. Nguyen, E. M. D'Amato, J. M. R. Narayanam, C. R. J. Stephenson, *Nat. Chem.,* **2012**, *4*, 854. (b) F. Teplý, *Collect. Czech. Chem. Commun.,* **2011**, *76*, 859. (c) J. Xuan, W.-J. Xiao, *Angew. Chem., Int. Ed.,* **2012**, *51*, 6828. (d) M. Majek, A. J. von Wangelin, *Angew. Chem., Int. Ed.,* **2013**, *52*, 5919. (e) M. Reckenthäler, A. G. Griesbeck, *Adv. Synth. Catal.,* **2013**, *355*, 2727. (f) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev*., **2013**, *113*, 5322. (g) T. P. Yoon, *ACS Catal.,* **2013**, *3*, 895. (h) Y. Xi, H. Yi, A. Lei, *Org. Biomol. Chem.,* **2013**, *11*, 2387. (i) M. A. Ischay, T. P. Yoon, *Eur. J. Org. Chem.,* **2012**, 3359. (j) L. Shi, W. Xia, *Chem. Soc. Rev.,* **2012**, *41*, 7687. (k) N. Hoffmann, *Chem. Sus. Chem.,* **2012**, *5*, 352. (l) J. W. Tucker, C. R. J. Stephenson, *J. Org. Chem.,* **2012**, *77*, 1617. (m) T. P. Yoon, M. A. Ischay, J. Du, *Nat. Chem.,* **2010**, *2*, 527.

4. D. Ravelli, M. Fagnoni, A. Albini, *Chem. Soc. Rev.,* **2013**, *42*, 97.

5. (a) L. Huang, J. Zhao, *RSC Adv.,* **2013**, *3*, 23377. (b) L. Huang, J. Zhao, *Chem. Commun.,* **2013**, *49*, 3751. (c) S. Guo, H. Zhang, L. Huang, Z. Guo, G. Xiong, J. Zhao, *Chem. Commun.,* **2013**, *49*, 8689. (d) J. Zhao, W. Wu, J. Sun, S. Guo, *Chem. Soc. Rev.,* **2013**, *42*, 5323.

6. (a) D. A. Nicewicz, T. M. Nguyen, *ACS Catal.,* **2013**, *4*, 355. (b) D. Ravelli, M. Fagnoni, *Chem. Cat. Chem.,* **2012**, *4*, 169. (c) Y. C. Teo, Y. Pan, C. H. Tan, *Chem. Cat. Chem.,* **2013**, *5*, 235. (d) D. Cantillo, O. de Frutos, J. A. Rincon, C. Mateos, C. O. Kappe, *Org. Lett.,* **2014**, *16*, 896.

7. (a) D. P. Hari, B. König, *Chem. Commun.,* **2014**, *50*, 6688. (b) D. Kundu, S. Ahammed, B. C. Ranu, *Org. Lett.,* **2014**, *16*, 1814. (c) D. P. Hari, P. Schroll, B. König, *J. Am. Chem. Soc.,* **2012**, *134*, 2958. (d) M. Majek, A. J. von Wangelin, *Chem. Commun.,* **2013**, *49*, 5507. (e) D.-T. Yang, Q.-Y. Meng, J.-J. Zhong, M. Xiang, Q. Liu, L.-Z. Wu, *Eur. J. Org. Chem.,* **2013**, 7528. (f) Q.-Y. Meng, J.-J. Zhong, Q. Liu, X.-W. Gao, H.-H. Zhang, T. Lei, Z.-J. Li, K. Feng, B. Chen, C.-H. Tung, L.-Z. Wu, *J. Am. Chem. Soc.,* **2013**, *135*, 19052.